CONTRIBUTION TO THE STUDY OF SARCOMA OF THE FEMUR.

PERIOSTEAL ROUND-CELLED SARCOMA OF THE FEMUR, INVOLVING TWO-THIRDS OF THE SHAFT, WITH VERY EXTENSIVE MULTIPLE METASTASES—APPARENT CURE BY THE MIXED TOXINS OF ERYSIPELAS AND BACILLUS PRODIGIOSUS. WELL 10½ YEARS, WHEN A MALIGNANT TUMOR (SARCOMA AND EPITHELIOMA) DEVELOPED IN THE THIGH AT THE SITE OF AN OLD X-RAY DERMATITIS.*

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THE patient who is the subject of this paper was shown before the New York Surgical Society on a number of occasions. A full report of the condition up to May, 1912, will be found in the November, 1912, number of the ANNALS OF SURGERY, p. 787. The case, at the time of publication, was, as far as I know, entirely unique, being the only one on record of a periosteal round-celled sarcoma of the femur, with metastases, cured by any method of treatment. Of 68 cases of periosteal sarcoma of the femur collected by Butlin, treated either by amputation at the hip-joint or just below the trochanter, only one was permanently cured (well eight years), and in this case there were no metastases. Since the earlier report of my case developments have occurred which render it of still greater interest.

When the patient came under my care in February, 1902, for sarcoma, periosteal, round-celled, involving two-thirds of the shaft (the diagnosis confirmed by microscopical examination by Dr. E. K. Dunham, Professor of Pathology of the Bellevue University Medical School), the involvement of the femur was so great that I advised immediate hip-joint amputation, which was refused by the patient. X-ray treatment was administered for a prolonged period, during which an extensive metastatic tumor occurred in the left pectoral region. A little later, a tumor the size of a child's head developed in the iliolumbar region, involving the ilium. The tumor of the pectoral region was partially removed and X-ray treatments for a short time after the operation were given. No X-ray was applied to the large iliolumbar tumor.

* Read before the American Surgical Association, May 7, 1913.

The toxins were given from February 12 to July 25, 1903, in doses ranging from .5 minim to 20 minims, 86 injections in all being given. The temperature rose to 103.5° F. As stated in the earlier history, the large iliolumbar tumor became almost completely broken down under two months' treatment with the toxins, and drainage was established by an incision made through the upper and posterior part of the ilium, and a large quantity of necrotic tissue evacuated. The patient went on to complete cure and remained well over ten years. Aside from the persistent dermatitis which followed the irritation from the X-ray, in the lower and anterior portion of the thigh, there was also some slight dermatitis in the pectoral region. At the time the patient was shown before the Surgical Society, in April, 1912, a small tumor, the size of an olive, had just developed in the pectoral region at the site of the dermatitis described. This was removed under cocaine the following week and pronounced epithelioma by Dr. Jas. Ewing, Professor of Pathology of Cornell University Medical School, without any connection whatever with the original sarcoma. The patient remained well during the summer, but in the latter part of October, 1912, when I again saw him, I found a very remarkable change had taken place in the old dermatitis in the lower part of the thigh. There was a very large ulcerating area, fully 10 inches in diameter, which showed unmistakable evidence of malignant degeneration, the discharge having the foul odor characteristic of epithelioma. The ulceration rapidly extended in all directions until it covered an area fully 12 x 12 inches and was constantly increasing in thickness. The general health of the patient also became greatly deteriorated. The appearance of the surface of the tumor was extremely characteristic of the tumors which I have seen originate in old X-ray burns. The disease in this case apparently started in the skin and subsequently involved the deeper layers, instead of beginning in the bone and spreading externally. This fact was distinctly shown by the X-ray photograph. The structure of the tumor proved to be very unusual, and different diagnoses were made by several pathologists, although the tumor was regarded by all as highly malignant. I am fortunate in having been able to obtain the following very clear and full report from Dr. W. H. Welch, professor of pathology of John Hopkins University:

Examination of Fragments of Tumor for Dr. W. B. Coley (Nov. 27, 1912).—The specimen consists of several small irregular, rather ragged fragments of solid tissue, the largest being about 2 cm. long, 1.5 cm. broad and 0.6 cm. thick. Upon two of the pieces epidermis can be recognized along one margin.

The microscopical sections show a neoplasm composed of cells and stroma, the former predominating. Some of the sections show only the tumor tissue; others present upon the edge of the tumor an ulcerated surface covered with fibrin, leucocytes and red corpuscles, and two sets of section show cutaneous tissue covered by a thick layer of epidermis. In these last sections the subcutaneous tissues are occupied by the tumor, which has evidently invaded the corium from below and in places appears to have reached the epidermal layer.

The tumor is composed mainly of cells with, as a rule, rather scanty fibrous stroma. The cells vary in size and shape but spherical, oval and polyhedrical cells of rather larger size with large vesicular nuclei, containing nucleoli, and with abundant cytoplasm, predominate. There are also fusiform cells, often occurring in bundles, cells with irregular nuclei and with two, three or more nuclei are common. In some fields the cells are closely compacted, while in others there is more of delicately fibrillated or even coarsely fibrous connective tissue between the cells. There is no marked tendency to arrangement of the cells in nests or alveoli.

While considerable parts of the tumor show no evidence of degeneration or marked inflammatory infiltration, there are areas which are extensively invaded with polynuclear leucocytes and lymphocytes, and here the nuclei of the tumor cells often stain diffusely or show other evidences of regressive changes. In parts not thus invaded nuclear figures are numerous.

In the sections presenting a covering with skin, the deeper layers, corresponding to the subcutaneous tissue, show a sarcomatous growth of essentially the characters already described, but in most places extensively invaded with leucocytes.

In the dense fibrous tissue of the corium, in which sections of small hair follicles are numerous, there are scattered strands and islands of richly cellular tissue. The typical large tumor cells can occasionally be seen in these cellular foci, but many of the cells are smaller and appear to lie in and around blood and lymph capillaries, the endothelium of which is swollen and proliferating. The majority of cells in these foci appear to be lymphocytes and plasma cells.

The epidermis is moderately infiltrated with wandering leucocytes. There is some thickening and down growth of the interpapillary processes of epithelium, and over an area of about one millimetre in extent in the sections, where the cellular infiltration of the corium is most extensive beneath the epidermis, there is such an irregular and considerable down growth of the epidermal cells as to suggest an epitheliomatous growth.

Diagnosis.—Large round-celled sarcoma.

There is no objection also to the designation of mixed-celled sarcoma, although the round-celled type predominates. The type is like

that of many periosteal sarcomata, as is indicated by the large cells with irregular and multiple nuclei. The specimen is evidently from metastases invading the skin, if, as I understand from the clinical history, the primary growth was of the periosteum.

While much of the tumor shows the ordinary appearances of sarcoma, it is interesting to note the considerable areas undergoing degeneration and especially the extensive infiltrations with leucocytes.

The interpretation of the lesions of the corium and epidermis over the subcutaneous sarcoma is not so obvious. While occasionally cells resembling the sarcoma cells are seen in the cellular foci of the corium, especially those nearest the subcutaneous growth, many of these foci appear to consist of capillaries with swollen and proliferating endothelium and of accumulations of lymphoid and plasma cells, so that these lesions are probably best interpreted as in the main of a chronic inflammatory character, that is a dermatitis.

The question as to the interpretation of an apparently invasive down growth of epidermal cells, as described above, can hardly be positively answered. Inasmuch as atypical down growths of cutaneous epithelium with inflammations and ulcers of the skin are common and sometimes extensive, it is possible that this is the correct interpretation of the lesion in this case. Still I should not be willing positively to exclude the possibility of a true epitheliomatous growth superimposed upon the sarcoma. The main growth, however, is, as described, a round-celled sarcoma of the type most frequently originating in the periosteum or endosteum (peripheral or central sarcoma of bone).

Pathologist, William H. Welch.

Taken from Dr. Welch's letter dated December 23, 1912:

"I spoke to Dr. Halsted about your specimen. He was extremely interested, and thought that the evidence for efficacy of the treatment by your method was strikingly manifested by the history of the case, and so it seems to me. To have brought about the disappearance of the tumor and to have kept the growth in check for ten years, and then to have the same (presumably) type of growth reappear in the original site and this a markedly malignant type of sarcoma, is a unique chain of events, which is perhaps more convincing than the disappearance of a tumor without a later return. I have not expressed this very clearly I fear, but you will see the point as it impressed Halsted.

(Signed) WILLIAM H. WELCH."

(Professor of Pathology at Johns Hopkins University, Baltimore.)

I also obtained reports on the tissue removed, from Dr. Jas. Ewing, professor of pathology, Cornell University Med. School, and Dr. W. C. Clark, pathologist at the General Memorial Hospital. Their reports are as follows:

"The tissue in the A. G. case shows intact epithelial lining; extensive œdema in many pockets. The derma is the seat of productive

new growth of tissue which, in many places, is composed of cellular and mucoid material. Many spindle- and star-shaped cells—large or huge hyperchromatic nuclei. Such areas grade insensibly into new cellular tissue in which the structure resembles that of large spindle-celled sarcoma. Here the cells are very numerous, large nuclei hyperchromatic, blood-vessels numerous. Parts of these areas are traversed by numerous elongated blood sinuses lined by spindle tumor cells, and the whole process suggests great potentialities of independent growth. To call it sarcoma, seems to me to dismiss it inadequately, but the clinical course may very well be that of spindle-celled sarcoma.

(Signed) J. EWING."

Dr. William C. Clark's report reads as follows:

Tumor of skin of leg, December 21, 1912. Patient, A. G.

Gross examination shows a mass projecting slightly above surrounding skin level. This mass is sharply outlined, measures a cm. in diameter, it is roughened and much firmer in consistency than the surrounding tissues.

On cut section the tumor is found to be sharply outlined, is oval and measures 6 cm. in depth.

Microscopic examination shows that the tumor is a part of the true skin, that is, the epithelial structures of the true skin become a part of the tumor.

The tumor proper consists of large epithelial cells of the squamous variety with relatively large deeply staining nuclei. This is especially true of the cells on the deeper part of the tumor.

The epithelial cells of the central and superficial parts of the tumor are pale, with pale nuclei. At one point in the epithelium there is a small cyst. The periphery of the tumor in contact with the deeper tissues is made up of rounded masses, and columns of epithelial cells, but the general outline of the tumor is sharp, clean cut and is not infiltrating the surrounding tissues. There is an extensive round-celled infiltration. There is no sign of ulceration.

Diagnosis.—Epithelioma of the basal-cell type.

I advised amputation of the leg as soon as the diagnosis was made, but failed to get the patient's consent until January 2, 1913. He was anxious to have the toxins tried again, and they were administered regularly from November 18, to December 5, 1912, in doses ranging from .5 minim to 5 minims, 12 injections in all being given, with no apparent effect upon the progress of the disease. The surface of the tumor was also treated with large doses of very strong radium ointment, principally in the hope of overcoming the very foul odor from the discharges. No effect was noted, however.

He also had one injection of colloidal copper. In view of the patient's failing general health and weak condition, all treatment was abandoned.

Later History.—After the case was reported before the Surgical Society, December 11, 1912, the patient's general condition continually grew worse, and his consent to have the leg sacrificed was finally obtained. On January 2, 1913, I amputated under nitrous oxide gas and oxygen. The entire operation, including the closing of the wound, took 13 minutes. Although the larger nerves were not cocainized, he showed very little shock from the operation, no nausea or vomiting and made a very good recovery. The limb was taken to the laboratory of Cornell Medical School and Dr. Ewing made a further study of the tumor. His second report reads as follows:

Case of G., April 23, 1913. Tumor of femur. Specimen consists of a leg amputated through the upper third of the thigh. The skin is absent over the anterior and lateral surfaces of the region of the knee-joint for a distance of 20 cm., and in its place is a hard nodular growth, pale in color and spotted here and there with ecchymotic areas varying in size from a pin point to 4 and 5 cm. in diameter, and small ulcerating areas (.5 to 1.5 cm.) containing white cheesy-like material.

On vertical section the tendon and lower portion of the rectus femoris, to within 2 cm. of the patella, is replaced by a tumor mass for a distance of 14 cm. This mass appears quite separate from the periosteum of the femur, a layer of fat being interposed. At its widest point it measures 6 cm. Its upper surface is covered with skin and subcutaneous fat, but the remaining portion has broken through the integument and produces an ulcerating area which is seen on the surface of the limb. The surface of this mass is smooth, white and glistening.

At the point of amputation, the diameter of the femur is not increased and the compact bone appears to be normal; the medullary cavity contains a reddish-brown marrow. In the lower third of the bone, it measures about 7 cm. in diameter and the medullary cavity has entirely disappeared; the compact bone is atrophied, in places being only a shell. Where the normal marrow cavity ends, there is a small deposit of cancellous bone; just below this, there are two bone cysts, measuring .5 and 1.5 cm. in diameter and lined with a glistening membrane. Extending from the cancellous bone, posterior to the cysts, is a mass of ivory-like compact bone which takes in the entire diameter of the femur just below the cysts. Below this compact bone is a sequestrum, 4.5 cm. in length, the remains of what appears to have been a part of the shaft of the

femur; this lies in cancellous tissue. Just above this condyle in the medullary cavity is a well circumscribed tumor measuring 5 × 3 cm.

The cut surface is white and granular in appearance and cuts with considerable resistance; the edges are well marked and the tumor does not appear to infiltrate the surrounding tissue.

The cancellous tissue in the condyles appears normal. Patella shows osteoporosis. The head of the tibia shows atrophy of compact bone. Medullary cavity is normal, except for an area 5 cm. long by 3 cm. wide, in which the marrow appears to be denser than the surrounding tissue.

Microscopical.—The compact tumor measuring 5 × 3 cm. in the marrow cavity of the lower end of the femur, is an adult acanthoma (epithelioma). It is composed of compact masses of stratified squamous epithelium of adult type, with spines and pearls and many large, almost cystic areas of hornified material. The stroma is cellular connective.

The tumor in the rectus femoris is composed of many large and small polygonal and spindle tumor cells, with vesicular hyperchromatic nuclei and prominent nucleoli. These cells invade the muscle tissue in rows, small groups, and diffusely. Muscle cells undergo simple atrophy.

The origin and nature of this tumor, I am unable to determine. It appears to be of rapid growth and of recent date. Its structure would ordinarily be designated as sarcoma. I do not think it arises from the femur, since the underlying periosteum is intact and separated from the tumor by a layer of fat tissue. The sequelæ of the original process in the bone are probably to be found in the cysts, the areas of osteosclerosis, and the large sequestrum mentioned in the gross description. It is difficult to determine whether or not these gross lesions can be interpreted as the result of an arrested sarcoma. It would seem possible that they might result from an old osteomyelitis with formation of sequestrum, osteosclerosis and bone cysts.

The epithelioma in the medullary cavity may be interpreted as a metastasis from a lesion in the skin resulting from the X-ray, but no such tumor was recognized in the ulcerated surface of the amputated specimen. It is very probable that the tumor of the quadriceps was an extension from the peculiar process in the ulcerated superficial tissues and that it resulted from the long use of the X-ray.

One to two weeks after the operation the patient developed metastases in the lung and probably also the peritoneum, and died on January 16, 1913.

Blood Analyses.—The various blood counts in this case are of interest:

November 6, 1912: W. B. C. 15,000; hæmoglobin 70 per cent.

December 12, 1912: W. B. C. 20,000; R. B. C. 3,000,000; hæmoglobin 60 per cent.

December 19, 1912: Hæmoglobin 50 per cent.

December 28, 1912: Hæmoglobin 60 per cent.

January 2, 1913: Hæmoglobin 50 per cent.

January 11, 1913: Hæmoglobin 35 per cent.

January 14, 1913: Leucocytes 106,000; polynuclears 99.5 per cent.; mononuclears 0.51 per cent.

January 16, 1913: Hæmoglobin 25 per cent.

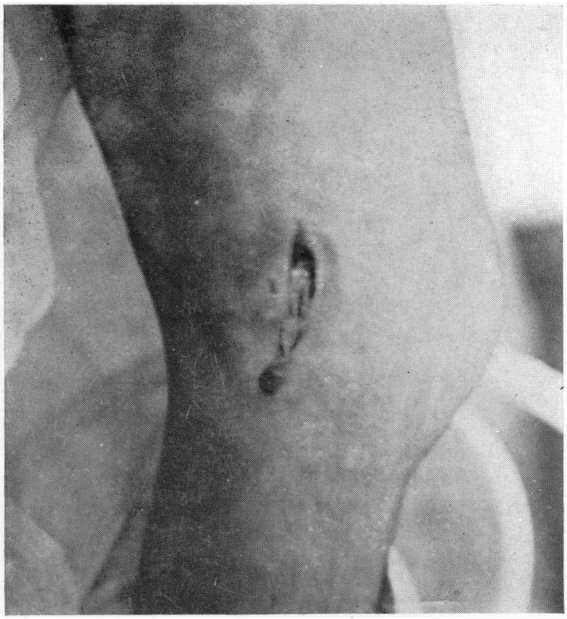
On consulting my records, I find an old report of a blood examination, dated May 5, 1902, at which time he was taking X-ray treatment for the periosteal sarcoma of the femur. The report reads as follows: Hæmoglobin 47 per cent.; red cells 3,300,000; white cells 11,100; lymphocytes 11 per cent.; polynuclear 69 per cent., of which 50 per cent. neutrophilic; mononuclear 10 per cent., disintegrating; eosinophiles 2 per cent., multinuclear; myelocytes (small) 8 per cent.

A careful study of the blood changes in bone carcinoma with metastases, has been recently made by Gordon R. Ward (*Lancet*, March 8, 1913, p. 676) based upon four cases. In these cases the hæmoglobin varied between 32 and 115 per cent., the white blood corpuscles in the four cases were 3700, 9000, 1080 and 15,000. The polynuclears varied between 48 and 53 per cent.

The facts in this case have been presented as clearly and judicially as possible; their interpretation will be left largely to the readers. It is unfortunate that the slide of the original specimen removed from the periosteal tumor of the femur in February, 1902, has not yet been found. In moving the laboratory of the General Memorial Hospital the index of the slides for this particular period was lost. Clinically and macroscopically, the appearance of the tumor was that of a periosteal tumor, involving two-thirds of the shaft of the femur, quite characteristic of sarcoma. A specimen was removed by a large exploratory incision and the diagnosis of small, round-celled sarcoma made by Dr. E. K. Dunham, director of the Carnegie Laboratory, and professor of pathology at Bellevue University Medical School, and by Dr. B. H. Buxton, Assistant Pathologist to the General Memorial Hospital. The subsequent history of the case, I believe, renders the loss of the slide unimportant, except for the purpose of making a comparison of the type of the tumor originally found, and the one that developed ten years later. The extensive multiple metastases which soon developed, confirm beyond question the diagnosis of malignant tumor.

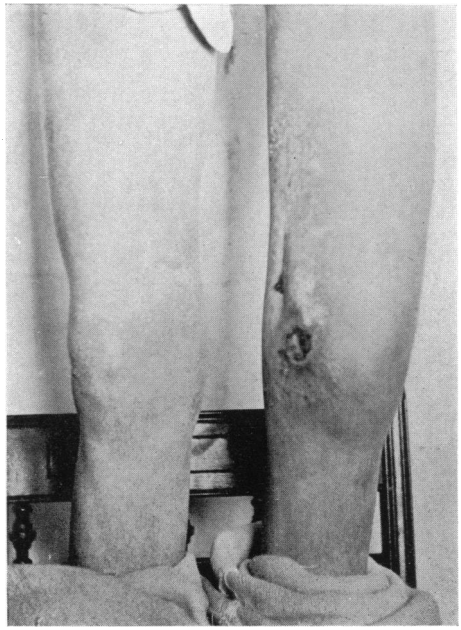
Conclusions.—My own conclusions after a careful study of all the clinical data in this case, together with the elaborate

FIG. 1.



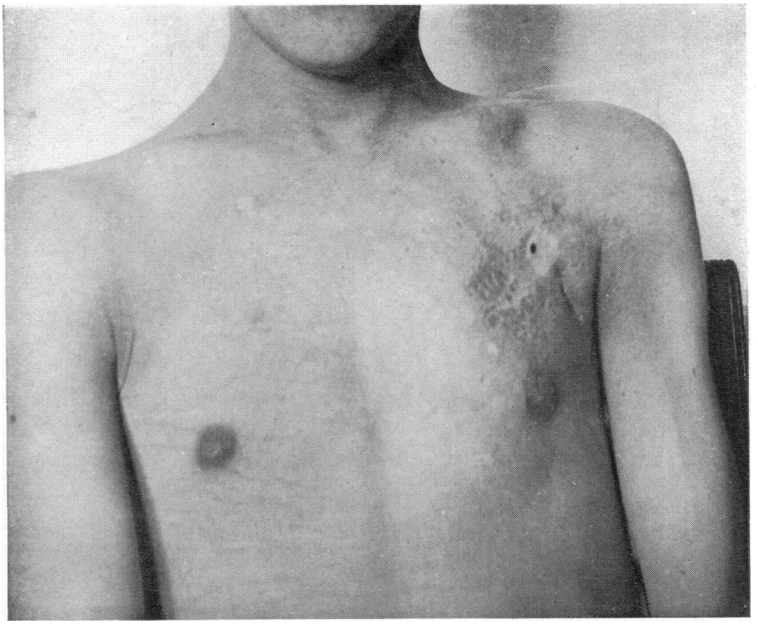
Sarcoma of left femur before treatment. Subperiosteal round-celled. Showing exploratory incision made in February, 1902. Under X-ray treatment developed extensive metastasis in left pectoral region and right iliolumbar region. Apparent cure by mixed toxins of erysipelas and bacillus prodigiosus. Patient well ten years later.

FIG. 2.



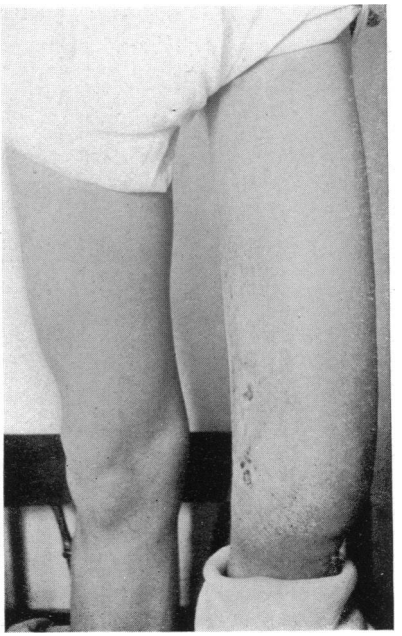
Sarcoma of femur, after six months' X-ray treatment.

FIG. 3.



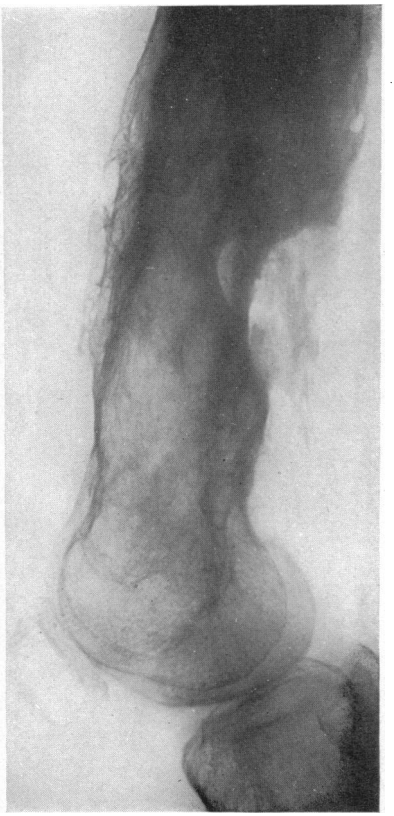
Sarcoma of femur. Metastasis in pectoral and lumbar regions. Showing dermatitis after X-ray treatment and site of epithelioma which developed ten years later.

FIG. 4.



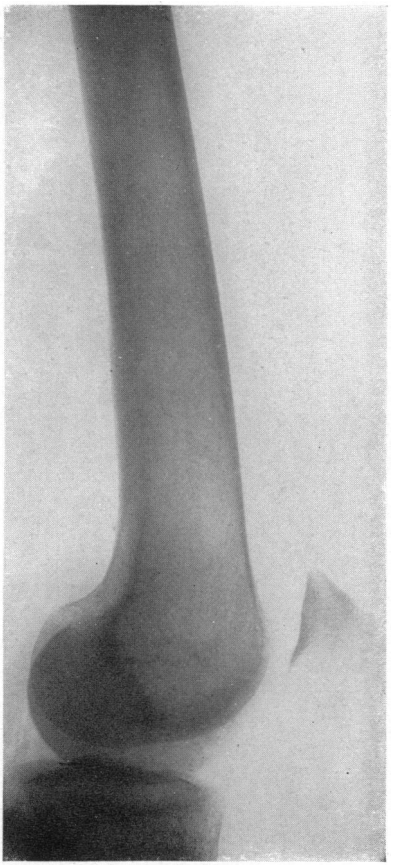
Appearance September, 1911.

FIG. 5*a*.



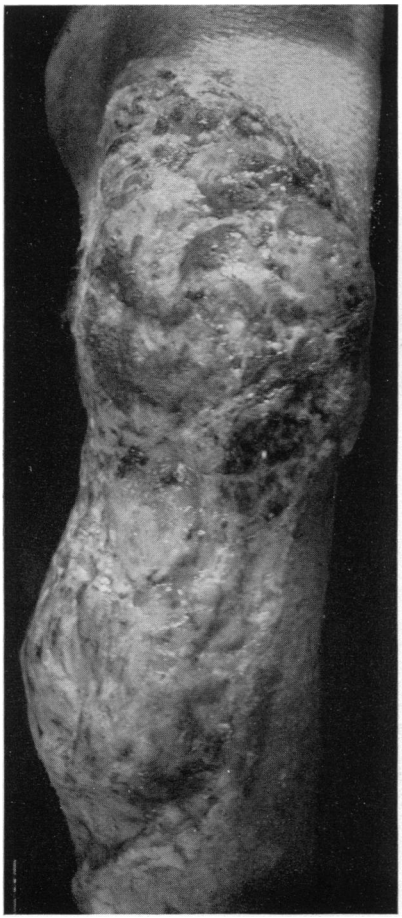
X-ray taken ten years after beginning of treatment, showing sequestrum and new formation of bone.

FIG. 5*b*.



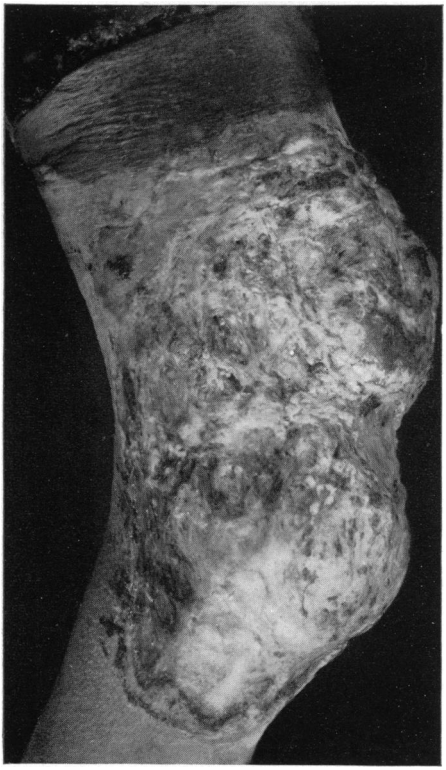
Sound femur.

FIG. 6.



November, 1912. Malignant tumor. Sarcoma and epithelioma at site of X-ray dermatitis, in thigh.

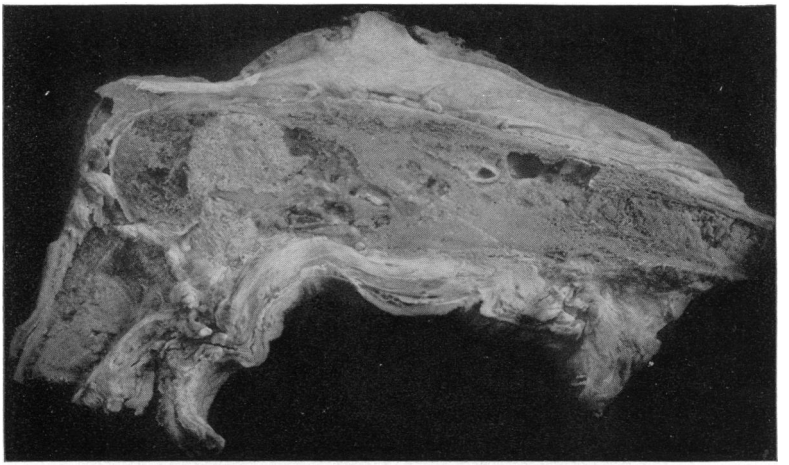
FIG. 7.



January 2, 1913. Showing rapid progress of disease in two months and appearance at time of amputation.

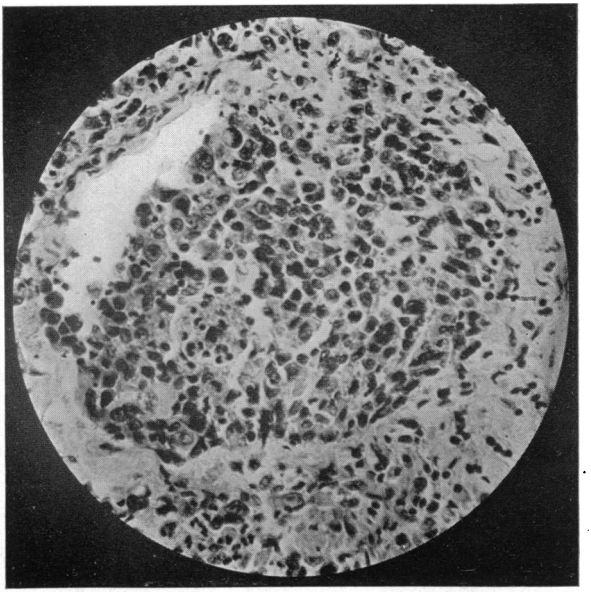
FIG. 8.

a. Intramedullary epithelioma



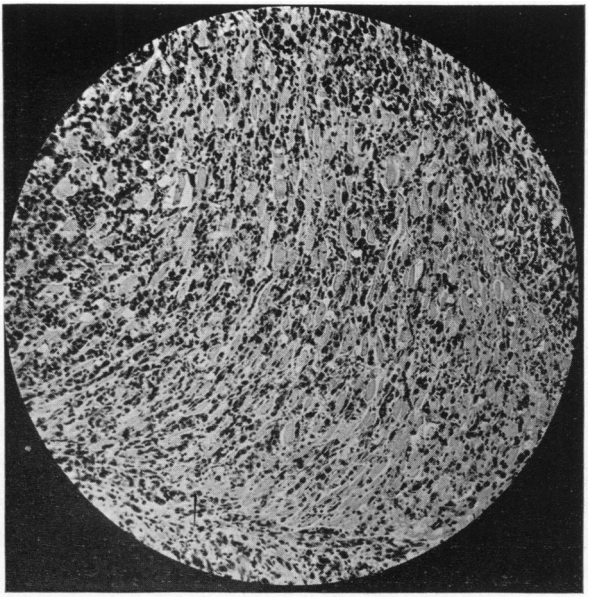
January, 1913. Longitudinal section showing large intramedullary epithelioma. Also bone cyst and sequestrum.

FIG. 9.



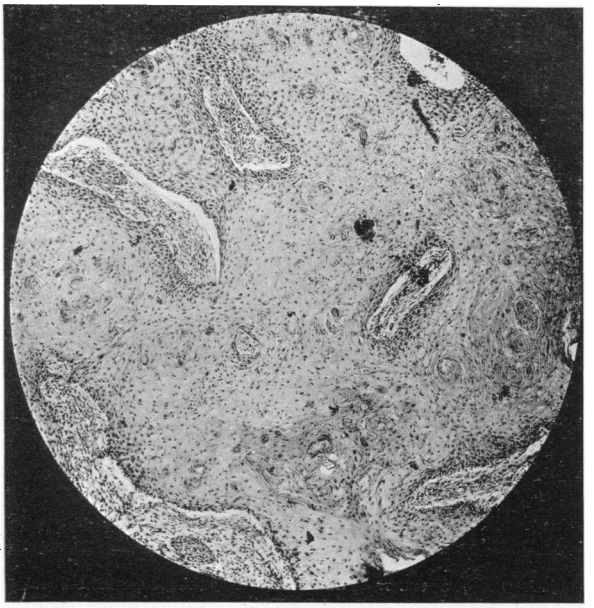
November, 1912. External tumor of thigh, involving skin and muscles (sarcoma and epithelioma).

FIG. 10.



November, 1912. External tumor of thigh, involving skin and muscles (sarcoma and epithelioma).

FIG. 11.



January 2, 1913. Intramedullary tumor (epithelioma).

reports of the microscopical findings by such competent men, are, that the malignant tumor which developed in the pectoral region in April, 1912, which was undoubtedly epithelioma, was a simple example of ordinary X-ray cancer occurring at the site of an old dermatitis of ten years before. The later tumor which developed in the thigh, in the autumn of 1912, started in a similar, but much more severe X-ray dermatitis, following X-ray burns of ten years before. This was of a much more highly malignant nature and grew with very great rapidity. The fact that it started in the skin and never—even at the time of death—reached the periosteum, strengthens the opinion that it was a new and independent tumor resulting from X-ray burns, and having no connection with the original periosteal sarcoma of ten and a half years earlier, which had apparently entirely disappeared. The earlier tumor never involved the skin or muscles, and the later tumor never invaded the bone or periosteum, except the metastatic tumor in the medullary cavity which proved to be an epithelioma. Part of the thigh tumor showed, according to Welch and Ewing, structures which must be classed as sarcoma. Other portions of the tumor showed, according to Clark, typical basal-celled carcinoma, while the intramedullary tumor was clearly epithelioma. It would appear then that we were dealing with different types of malignant disease—sarcoma, carcinoma—in the same individual and approximately at the same locality, resulting directly or indirectly from chronic irritation caused by X-rays. Therefore cysts and sequestra are easily explained as the result of a rather extensive chronic osteomyelitis following the breaking down of the sarcoma of the femur under the influence of the X-rays and toxins and infection from the sinus which persisted after the large exploratory incision. I have known of one other case, reported by one of the German clinics, of an X-ray worker, in which two different types of malignant tumor (one a sarcoma and the other carcinoma) occurred in the neighborhood of the wrist, following a dermatitis produced by exposure to the X-rays. The two types of tumor occurred within two inches of each other. (The reference to this case I am unable to find.)

We are all familiar with the experimental production of sarcoma in the rat, by Marie and Clunet, published in the *Second International Congress for Cancer Research,* Paris, 1910. These investigators set out deliberately to produce a malignant tumor by producing a series of X-ray burns in the same locality, pushing the exposure to the point of ulceration, and when this had healed, repeating the experiment 4 to 5 times. At the end of this time, typical sarcoma developed at the site of the exposures.

The exact method by which X-rays produce a malignant tumor is not known. It would be idle to enter into any prolonged attempt to theorize on this question in the present paper.

I believe that X-ray cancer throws little light upon the great problem of the etiology of malignant tumors in general. It adds little to the evidence for or against the extrinsic or microbic origin of the disease. Personally, I believe it can be better explained by the parasitic theory than by any of the cellular or intrinsic theories. We should simply have to assume the existence of a widely disseminated and very generally present microörganism or virus to which nearly every individual is exposed, and yet, which under normal conditions will be successfully withstood by the resisting powers of the tissues. Under certain unusual or abnormal conditions, such as bruising of the tissues resulting from trauma, or the changes caused by chronic irritations of various sorts, including those occasioned by the X-ray, these tissues lose their normal resisting power and furnish a favorable site or nidus for the microörganisms. When once these have obtained a foothold, it will be found very difficult to control or eradicate them.

Some of those who find it difficult to explain the origin of X-ray cancer on the microbic theory, assume that the infectious agent reaches the site of development by reason of abrasions or cracks or external ulceration. If this were true, it would be hard to explain the development of cancer in cases in which there was no ulceration.

My theory is entirely different, in that I believe the infection reaches the particular locality through the blood supply, just as localized tuberculosis of bones or joints in children develops after a trauma, without any external abrasion. In these cases we must assume a latent organism present in the system, remaining harmless until the trauma so lowers the vitality of the tissues as to furnish a favorable nidus for the organism coming through the blood to gain a foothold.

Hesse, of the University Poliklinik of Bonn (*Zwanglose Abhandlungen aus d. Gebiete d. Med. Elektrologie und Roentgenkunde, Hft.* 10, 1911), has made, I believe, the most careful study of the X-ray cancer up to the present time.

Of 90 positively determined malignant tumors following the exposure to X-rays, occurring in 54 patients, 5 or 5.5 per cent. were tumors resembling fibrosarcoma. Only one was a spindle-celled sarcoma as proven by histological examination. Hence, there was but one positive Röntgen sarcoma in the entire series.

Of 94 Röntgen lesions reported, 54 were cases of uncomplicated carcinoma, including one case of sarcoma, the latter in conjunction with "cancroids"; in 13 cases the diagnosis was not absolutely certain or there were other complications; and 27 carcinomas in cases of X-rayed lupus. Twenty-six of the positive cases were observed in America, 13 in Germany, 13 in England and 2 in France.

Hesse brings out the important point that Röntgen carcinoma never develops as a simple or primary injury due to raying, but exclusively in the soil of an already present Röntgen injury.

As regards the etiology of Röntgen carcinoma, he believes that one should certainly consider the possibility of their being due to some kind of infection, either bacterial or protozoic. He states that the skin, which has been exposed to the X-rays, is full of cracks and ulcers, often as thin as tissue paper, and with little or no power of resistance, offers a favorable soil for the entrance of foreign organisms.

Against the infectious theory, he mentions the fact that

in some patients the carcinoma develops in cicatrices that had not shown any sign of inflammation for a long period, in which cases one would have to assume that the cancer germs had remained latent in the tissue and then had become active for some unknown reason. Nevertheless, he states, the infectious theory cannot be excluded.

With reference to therapy, he believes that limited success may be obtained by symptomatic treatment. He adds "The Röntgen carcinoma itself cannot be treated radically enough, and the soil of the carcinoma cannot be treated mildly enough."

Referring to the prognosis, he states that without treatment the carcinoma invariably causes the death of the individual afflicted. Under treatment the cancer as such may be cured but a *restitutio ad integrum* is impossible. A complete cure of the xeroderma pigmentosum does not occur, although attempts to bring the same to a stage where it will cease to further generate carcinoma, may be successful.